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| 10/644,587 | 08/20/2003 | Connie Sanchez | 05432/100M919-US4 | 5266 |

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| EXAMINER | |
|---|---|
| ISSAC, ROY P | |
| **ART UNIT** | **PAPER NUMBER** |
| 1623 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
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| 3 MONTHS | 02/02/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/644,587 | SANCHEZ ET AL. | |
| | Examiner | Art Unit | |
| | Roy P. Issac | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *20,22-25,27-30 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,22-25,27-30 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/11/06; 9/28/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This application claims priority under 35 U.S.C 119 from foreign filed application PA 2001 00684, filed May 1, 2001.

This Office Action is in response to Applicant's amendment/ remarks/ response filed 11/15/2006 wherein claim 20 was amended and new claims 21, 26 and 31 were cancelled. Claims 20, 22-25, 27-30 and 32-34 are currently pending, and under examination on the merits.

### *Rejections Withdrawn*

The rejection under 35 U.S.C § 112, second paragraph with respect to the term "less" of claims 20 is withdrawn, since claim 20 has been amended to remove the term "less" and to specify the daily dose of 2.5 to 10.0 mg of escitalopram.

As indicated above, applicant's arguments/response filed 15 November 2006 cancelled claims 21, 26 and 31. All rejections made with respect to the cancelled claims in the previous office action are withdrawn.

The terminal disclaimer filed on 11/15/2006 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of Application No. 10/468,685, and Application No. 10/644,588 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 11/15/2006 with respect to the rejection of claims 20-34 made under the judicially created doctrine of obviousness-type

double patenting as being unpatentable over claims 21, 23, 25, 27, 29, 31, 33, 35 and 37 of U. S. Application No. 10/644,588 and over claims 36-46 of U.S. Application No. 10/468,685 of record in the previous Office Action dated 05/15/2006, has been considered and found persuasive. Therefore, this obviousness-type double patenting rejection is withdrawn.

Applicant's arguments, see pages 4-5, filed 11/15/2006, with respect to the rejection(s) of claim(s) statutory double patenting under 35 U.S.C § 101 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the pending claims.

Applicant's arguments, see Pages 5-6 titled "Anticipation Rejections", filed 11/15/2006, with respect to the rejection(s) of claim(s) 20, 22, 24, 25, 27, 29, 30, 32 and 34 under 102(b) over Boegesoe et. al. have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the pending claims.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In*

*re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20, 22-25, 27-30 and 32-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20-40 of copending Application No. 10/644,579 in view of Merck Manual. (Page 440, Column 2, paragraph 2; PTO-892, Cited by the examiner). Although the conflicting claims are not identical, they are not patentably distinct from each other because the'579 application claims a method of treating depression in a patient who failed to respond to initial treatment with an SSRI by the administration of escitalopram. The instant application claims a method for the treating depression in a patient suffering from depression who has a sleep disturbance when treated with a SSRI other than escitalopram. Sleep disturbances are well known to be associated with depression and the treatment of severe depression will include those with sleep disturbances associated with depression. Merck manual of diagnostics note that, "Most depressed people have difficulty falling asleep and awaken repeatedly particularly early in the morning." (Page 440, Column 2, paragraph 2; PTO-892, Cited by the examiner).

It would have been obvious to one of ordinary skill in the art to use escitalopram to treat major depression and those with sleep disturbances due to depression.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20, 22-25, 27-30 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment with respect to amended claims herein has been fully considered but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for a "daily dose of 2.5 to 10 mg". The original specification clearly discloses "dose of 10 mg" (Page 3, lines 22-26), "daily doses lower than 10 mg" (Page 5, lines 32-34), and a unit dose preparation of 2.5 to 20 mg. (Page 5, lines 29-30). The range now claimed "daily dose of 2.5 to 10 mg" is considered to the subgenus range of "dose preparation of 2.5 to 20mg" as originally described. The court held that

"subgenus range was not supported by generic disclosure and specific example within the subgenus range"; See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971); the court also held that "a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads" (see *In re Smith*, 458 F.2d 1389,1395, 173 USPQ 679, 683 (CCPA 1972). See also MPEP 2163. Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in possession of the invention as it is now claimed. See *Vas-Cath Inc. v. Mahurkar*, 19 USPQ 2d 1111, CAFC 1991, see also *In re Winkhaus*, 188 USPQ 129, CCPA 1975.

Claims 20, 22-25, 27-30 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had full possession of the claimed invention.

The instant application claims a method of treating a patient suffering from depression who has a sleep disturbance when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbance comprising administering a daily pharmaceutically effective amount of escitalopram. The only mention of "sleep disturbances" in the application follows; "As a further advantage, the fact that escitalopram is effective in lower doses suggests that effective treatment with less side effects may be obtained, in

particular, a reduced amount of serotonin reuptake inhibitor **may reduce the risk of SSRI-induced sexual dysfunction and sleep disturbances**." (emphasis added). The disclosure is merely speculating that a lower dosage use *may* have beneficial effects. There is no showing of the use of escitalopram in any patients who have suffered from sleep disturbance. The claim herein is directed to "a patient suffering from depression who has **a sleep disturbance**". Here there is no showing that the patients have not suffered even one instance of "a sleep disturbance" as claimed herein. Thus, one of ordinary skill in the art would not believe that the applicant had full possession of the invention as claimed.

Claims 20, 22-25, 27-30 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of depression with escitalopram, does not reasonably provide enablement for a method of treating a patient suffering from depression who has a sleep disturbance when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbance comprising administering a daily pharmaceutically effective amount of escitalopram. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue

experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The instant application relates to a method for treating a patient suffering from depression who has a sleep disturbance when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing a sleep disturbance comprising administering escitalopram.

The relative skill of those in the art:

The relative skill of those in the art is high, with a typical practitioner having obtained a PhD, M.S. or equivalent advanced degree.

Breadth of the claims

The claims are deemed very broad since, the claim encompasses any patient who has suffered from *even one instance of depression* when treated with a SSRI other than escitalopram.

The presence or absence of working examples and the amount of direction or guidance presented:

The applicants disclose a clinical study for the treatment of **depression** using escitalopram and citalopram. (Page 6, lines 20-page 7). The study compared escitalopram and citalopram for **depression** using the MADRS scale. However, the study does not disclose the treatment of any patients suffering from depression who has a sleep disturbance when treated with an SSRI other than escitalopram without inducing a sleep disturbance. In view of any disclosure showing a treatment of ay patients suffering from depression who has a sleep disturbance when treated with an SSRI other than escitalopram without inducing a sleep disturbance, one of skill in the art will have to conduct extensive research efforts.

The predictability or lack thereof in the art and the quantity of experimentation necessary:

The disclosure do not contain any examples of the treatment of "a patient suffering from depression who has a sleep disturbance." There is no indication that any of the patients have had even used other SSRIs prior to entering into the clinical trials herein. As such, there is no indication that they suffered from sleep disturbances. The lack of working examples is a critical and crucial factor to be considered, especially in cases involving an unpredicatable and undeveloped art. See MPEP § 2164.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable

an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses thousands of compositions with varying effects and unknown side effects. As such, each composition will need to be individually evaluated for activity.

In order to determine how the patients can be treated without inducing even one instance of sleep disturbance, one of skill in the art will have to conduct extensive research including extensive intellectual input from highly trained scientists and medical doctors.

Thus, the specification fails to provide clear and convincing evidence in sufficient support for the treatment of a method for treating a patient suffering from depression who has a sleep disturbance when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing a sleep disturbance.

*Genentech*, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the *Wands* factors as discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in ***undue experimentation*** to practice the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22 is further rejected under 35 U.S.C 112, second paragraph, for the following reason. Claim 22 is directed to the use of a daily dose of 7.5mg or less of escitalopram. The specification does not define "less." The lack of lower limit in the claimed range renders the claim indefinite.

***Response to Arguments***

Applicant has not addressed the rejection under 35 U.S.C 112, second paragraph with respect to claim 22 in the response filed dated 15 November 2006.

The claim is deemed properly rejected under 35 U.S.C 112 second paragraph and is adhered to.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20, 22-25, 27-30 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boegesoe et.al. (U.S. Patent # RE 34,712) or Boegesoe et.al, (EP Publication # 0347066 B1, 1995) in view of Bouchard et.al. (PTO-1449, Of Record), further in view of Merck Manual. (Page 440, Column 2, paragraph 2; PTO-892, Cited by the examiner).

The '712 patent describes the synthesis and use of (+)-citalopram for depression. (Column 1, lines 13-35). The '712 patent discloses a method for using (+)-citalopram and its non-toxic addition salts, such as oxalate salt, and crystallization. (See Column 1, line 45-46). The '712 patent further teaches the use of a pharmaceutically effective amount of (+)-citalopram and discloses 5-50mg daily dosage, in particular 5mg. (See example at Column 9, line 10). Furtheremore, the '712 patent discloses a method for using (+)-citalopram and its non-toxic addition salts, such as oxalate salt, and crystallization. (See Column 1, line 45-46). The '712 patent further teaches the use of a pharmaceutically effective amount of (+)-citalopram and discloses 5-50mg daily dosage, in particular 5mg. (See example at Column 9, line 10)

Boegesoe et. al. does not expressly disclose the treatment of a patient suffering from depression who has a sleep disturbance when treated with a selective serotonin reuptake inhibitor other than escitalopram or the daily dose of 7.5mg.

Bouchard et.al.. teach the use of citalopram because of its low side effects in patients with depression. The authors note that; "Single MADRS-items analyses revealed a better effect of citalopram on "reduced appetite" on day 14 and 42, "apparent sadness", "reduced sleep" and "suicidal thought" on day 42." (Pg. 57, Col1, lines 32-40).

Merck manual of diagnostics note that, "Most depressed people have difficulty falling asleep and awaken repeatedly particularly early in the morning." (Page 440, Column 2, paragraph 2; PTO-892, Cited by the examiner).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a daily dose of 5-10mg, such as 7.5mg, of (+)-citalopram or its oxalate salt for the treatment of patients suffering from depression who have sleep disturbances when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbances.

One of ordinary skill in the art would have been motivated to treat patients with (+)-citalopram in daily dosage ranges of 5-10mg, including 7.5mg, for patients suffering from depression who have sleep disturbances when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbances, because citalopram has advantages as an antidepressant with low sleep disturbance and because citalopram's pharmacological activity is attributed to its (+)-citalopram enantiomer. The instant claimed range of 10mg or less overlaps with the 5-50mg disclosed in Boegesoe. If the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a

*prima facie* case of obviousness exits. See *In re Woodruff,* 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir 1990). See MPEP § 2144.05 [4-1].

Therefore one of ordinary skill in the art would have reasonably expected that the use of escitalopram for the treatment of patient suffering from depression who has a sleep disturbance when treated with a selective serotonin reuptake inhibitor would result in reduced sleep disturbance.

Thus, the claimed invention as a whole is clearly *prima facie* obvious over the combined teachings of the prior art.

***Response to Arguments***

Applicant's arguments filed 15 November 2006 with respect to this rejection of claims 21, 23, 26, 28 and 33 made under 35 U.S.C 103(a) of record in the previous Office Action have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art as further discussed below.

The applicants argue that there is no teaching, suggestion, or motivation in the cited prior art. However, the examiner has indicated the advantages described in Bouchard et. al. (Page 8, last paragraph), and the overlapping ranges disclosed in Boegesoe et. al. (Page 9, second paragraph).

Applicants argue that one of ordinary skill in the art would not have had a reasonable expectation of success for using escitalopram to treat depression without inducing a sleep disturbance in such a patient. Applicants argument was found unpersuasive, since Bouchard discloses that citalopram, the racemic

mixture that includes escitalopram had better effect on reduced sleep. Applicants cite Asnis et. al. to support their position that SSRIs often exhibited sleep disturbances. However, Bouchard clearly indicates that citalopram had better effects on reduced sleep. Bouchard's teaching in view of Asnis et. al. showing that SSRIs exhibited sleep disturbances one of ordinary skill in the art would have had a preference for using escitalopram in patients suffering from depression who has a sleep disturbance when treated with a SSRI other than escitalopram.

Rejection over Feigner et. al. in view of Hyttel further in view of Schoffers

Claims 20, 22-25, 27-30 and 32-34 are further rejected under 35 U.S.C. 103(a) as being unpatentable over Feighner, JP et. al. ( PTO-892, Of record), in view of Hyttel, J. et. al. (PTO-1449, Of record) further in view of Schoffers et. al. (PTO-892, Of record).

Feighner et. al disclose the use of racemic citalopram for moderate-to-severe depression in dosage levels ranging from 10mg to 60mg. One skilled in the art would recognize that a racemic mixture contains two enantiomers of a compound in its (+) and (-) form. The (+) and (-) designate the optical activity of the compound. Generally, a racemic mixture has both enantiomers in about equal proportions. Thus, a 10mg dose of racemic citalopram should contain 5mg of its (+) enantiomer and 5mg of its (-) enantiomer. The chiral dosage range of (+)-citalopram in Feigner's study is estimated to be 5-30mg. The authors also disclose the use of citalopram in patients who have been treated with other

antidepressants. (Page 826, Table 1, line 6). The study also shows a decrease in insomnia in patients treated with citalopram at lower dose levels. (Page 828, Table 3, line 3). The length of the study was six-weeks. (Page 824, Column 1, Paragraph 3).

Feighner et. al. does not disclose the use of the escitalopram ((+)-citalopram), as the applicant define that esctialopram refers to one of the enantiomers of *S*- or (+)-citalopram. (Specification, Page 1, line 3-5). Feigner et. al. does not disclose the use of oxalate salt or the oxalate salt in its crystalline form.

Hyttel et. al teach the use of (+)-citalopram, and its crystallized oxalate salt, and shows that the pharmacological activity of the racemic citalopram is attributed to one of its enantiomers, (+)-citalopram, also known as escitalopram. (See Pg.157, lines 10-14, and Pg. 158, lines 25-29).

Schoffers et. al teach the advantages of using chirally pure compounds as pharmaceuticals. The author notes: "An increasing interest in understanding biological processes and the general recognition that chirality plays a crucial role in nature fostered tremendous effort in enantioselective synthesis. In the course of synthesizing natural products and designing new target compounds, chemists had to acknowledge the fact that enantiopurity is related to biological processes. Opposite enantiomers interact differently within an organism and can display various activities." (See Page 3770, lines 3-12). Furthermore, the advantages of using chirally pure drugs are well known in the art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a daily dose of 5-10mg of (+)-citalopram or its oxalate salt for the treatment of patients suffering from depression who have sleep disturbances when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbances.

One having ordinary skill in the art would have been motivated to treat patients with depression who have sleep disturbances when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbances comprising administering a daily pharmaceutically effective amount of escitalopram, because decreasing dose levels in citalopram leads to reduced side effects, and it is effective in daily dose ranges of 10-60mg or 5-30mg of (+)-citalopram. One skilled in the art would be further motivated to use (+)-citalopram or its oxalate salt because of the advantages of using a chirally pure drug and due to Hyttel's showing that the pharmacological activity resides in (+)-citalopram enantiomer. The instant claimed range of 10mg or less overalps with the 10-60mg (5-30mg chiral dosage) disclosed in Feigner. If the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exits. See *In re Woodruff,* 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir 1990). See MPEP § 2144.05 [4-1].

Therefore one of ordinary skill in the art would have reasonably expected that the use of escitalopram for the treatment of patient suffering from depression who has a sleep disturbance when treated with a selective serotonin reuptake inhibitor would result in reduced sleep disturbance.

Thus, the claimed invention as a whole is clearly *prima facie* obvious over the combined teachings of the prior art.

***Response to Arguments***

Applicant's arguments filed 15 November 2006 with respect to this rejection of claims 20-34 made under 35 U.S.C 103(a) of record in the previous Office Action have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art as further discussed below.

Applicants argue that there would have been no motivation to select escitalopram for the treatment of a patient suffering from depression who has a sleep disturbance when treated with an SSRI other than escitalopram. However, Feigner et. al. discloses reduced sleep disturbances in patients treated with citalopram and escitalopram is the enantiomerically pure active isomer of citalopram. Furthermore Hyttel et. al. discloses the use of escitalopram in ranges overlapping the ranged claimed herein. As such, one of ordinary skill in the art would have been motivated to use escitalopram to treat patients suffering from depression who has a sleep disturbance when treated with a SSRI other than escitalopram.

No claims are allowed. This rejection is made NON-FINAL due to the new/modified grounds of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy P. Issac whose telephone number is 571-272-2674. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

1/31/07

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